

### **REMARKS**

Claims 12-20 are pending. Claim 12 represents the sole independent claim.

The first paragraph on page 1 of the specification has been amended to update the status of the parent application, Application No. 09/720384, which is abandoned.

A clarification of the sequence listing SEQ ID NO:3 and the region therein that encodes SEQ ID NO:4 was requested on Page 2 of the Office Action. The total length of the isolated cDNA consists of 1217 bp (SEQ ID NO:3) and is believed to encode a functional protein. A sequencing error eliminated a nucleotide at position 406, which resulted in a frameshift that eliminated the putative start methionine of the full length cDNA sequence. Applicants note that there is an ATG codon at position 137 of SEQ ID NO:4. The termination codon is localized at position 1032 (TAG). In addition, the 3' end includes a poly(A)<sup>+</sup> tail. Applicants provide Appendices A, B and C, which are sequence alignments of pertinent amino acid and nucleic acid sequences. Appendix A is a Clustal V alignment of SEQ ID NO:4 of the instant claims and the following three APS kinase proteins:

1. *Catharanthus raseus* APS kinase (SEQ ID NO:13 of the instant specification; GI 2832300).
2. *Arabidopsis thaliana* APS kinase (SEQ ID NO:14 of the instant specification (GI 1076283) and also found in Figure 2 of MacRae starting at amino acid 58).<sup>1</sup>
3. *Saccharomyces cerevisiae* APS kinase (found in Figure 2 of MacRae; GI 3529).

Appendix B is an alignment of the following amino acid sequences: SEQ ID NO:4, p0016ctscj40rb, and *Saccharomyces cerevisiae* APS kinase (GI 3529), which highlights the differences at the N-terminal end of the respective sequences of SEQ ID NO:4 and p0016ctscj40rb due to the sequencing error. Appendix C is an alignment of nucleic acid sequences of SEQ ID NO:3 and clone p0016ctscj40rb, which shows the missing nucleotide in SEQ ID NO:3 at position 406.

Claims 12-20 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well-established utility. In addition, claims 12-20 stand rejected under 35 U.S.C. 112, first paragraph, for lack of enablement because "the claimed invention is not supported by either a

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<sup>1</sup> Applicants believe SEQ ID NO:14 to contain a transit peptide, based on the disclosure in Arz at page 450 of a transit peptide in an *Arabidopsis thaliana* APS kinase separated by a VRACVS sequence from the core protein (in Appendix A attached hereto, see amino acids 35-40 of GI 1076283). Applicants believe that SEQ ID NO:4 of the instant claims contains at least a part of a transit peptide on the N-terminus.

substantial asserted utility or a well established utility for the reasons set forth above [in section 101 lack of utility rejection], one skilled in the art clearly would not know how to use the claimed invention."

The claimed invention does have a substantial utility because, although the encoded protein fragment SEQ ID NO:4 is not a complete protein, it does have enzymatic activity for the reasons discussed herein. SEQ ID NO:3 is a nucleic acid sequence that encodes a functional protein having APS kinase activity. The alignment set forth in Appendix B of the translation product for SEQ ID NO:3, SEQ ID NO:4, and the amino acid sequence of yeast APS kinase (GI:3529) shows that SEQ ID NO:4 has significant homology with the complete N-terminal end (and the remaining sequence) of yeast APS kinase. The yeast APS kinase was compared because it does not appear to contain a (plastid) targeting signal. The alignment indicates that the sequencing error caused a frameshift upstream of the mature protein, and affected **only** the plastid targeting sequence. This conclusion is supported by the Declaration of Dr. Mitchell C. Tarczynski, which is being submitted herewith.

Enclosed are the following references related to the enzyme adenosine 5'-phosphosulfate (APS) kinase:

Deyrup et al. (*The Journal of Biological Chemistry* 273 (16):9450-9456 (April 17, 1998) ("Deyrup")  
Satishchandran et al. (*Biochemistry* 31:11684-11688 (1992) ("Satishchandran")  
Arz et al. (*Biochimica et Biophysica Acta* 1218:447-452 (1994) ("Arz")  
MacRae et al. (*Biochemistry* 39:1613-1621 (2000) ("MacRae"))<sup>2</sup>

Deyrup identifies the active site P-loop as a common structural feature of APS kinase activity. See also Figure 2 in Satishchandran and Figure 1 in Arz, and Figure 2 in MacRae. Furthermore, Satishchandran (Figure 2), Arz (page 449), and MacRae (Figure 2) also disclose the (P)APS binding region. The active site P-loop and binding (P)APS motif in the four sequences aligned in Appendix A are identified by boxes and are highly conserved in all four sequences. The existence of these conserved motifs in SEQ ID NO:4, combined with the frameshift error that appears to affect only the N-terminal plastid targeting sequence, provides further evidence that SEQ ID NO:4 is a functional APS kinase.

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<sup>2</sup> Although MacRae has a publication date after the earliest filing date of the instant application, Applicants submit that MacRae represents the state of knowledge of one of ordinary skill in the art, as of the earliest filing date of the instant application, at least with respect to the active site P-loop and (P)APS motifs associated with APS kinase activity, since these same motifs are disclosed in Satishchandran and Arz, which have publication dates well before the earliest filing date of the instant application.

In view of the foregoing, withdrawal of the rejections of claims 12-20 under 35 U.S.C. 101 and 112, first paragraph (enablement) is respectfully requested.

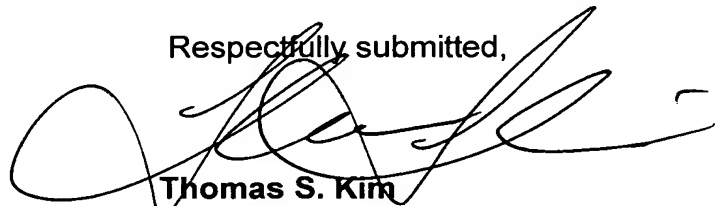
Claims 12-20 stand rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement.

It respectfully submitted that the above-discussion with respect to written description is equally apposite to this ground of rejection. As such, withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, for alleged failure to meet the written description requirement is respectfully requested.

In light of the foregoing, it is respectfully submitted that the claims are in condition for allowance and such allowance is respectfully requested. A Petition for a three-month extension of time, a Supplemental Information Disclosure Statement, copies of Deyrup, Satishchandran, Arz, MacRae, and the Plant Gene Register references, Declaration of Dr. Mitchell C. Tarczynski, and Appendices A, B and C accompany this response.

Please charge any fees or credit any overpayment of fees, which are required in connection herewith to Deposit Account No. 04-1928 (E.I. du Pont de Nemours and Company).

Respectfully submitted,



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